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13. ABSTRACT ***(Maximum 200 Words)***

This is a population based follow-up study of 145 African American (AA) and 177 white (W) women who were diagnosed with breast cancer between 1987 and 1989. As of January, 1999, 135 (41.9%) of the women had died with an average time to death of 4.7 years. Survival among AA women (56.9%) was significantly lower than survival in W women (68.9%) [age-adjusted Risk Ratio {RR} 1.73 (95% Confidence Interval {CI} 1.21 – 2.48)]. The significant survival disadvantage persisted even with additional adjustment for TNM stage at diagnosis and one measure of socioeconomic status (education) (RR 1.49, 95% CI 1.02 – 2.19). Several tumor characteristics differed by race group, with African American women more likely to be in the higher risk category. African American women were twice as likely to be diagnosed with tumors that were TNM stage II or higher (age-adjusted Odds Ratio [OR] = 2.01, 95% Confidence Interval [CI] 1.24 – 3.24). Evaluating archived tissue specimens, we have demonstrated race differences in a number of other tumor characteristics and genetic alterations: AA women were significantly more likely than W women to have tumors that were higher histologic grade higher nuclear), estrogen receptor negative, and p53 positive, all of which are associated with relatively poor prognosis. Although AA women were more likely than W women to be progesterone receptor negative (61% vs. 50%), and to express c-met (62% vs. 56%), these differences were not statistically significant. AA women were not significantly more likely to be HER-2 [neu] positive. African American women were more likely (not significant) to be positive for a number of known prognostic indicators: necrosis, lymphatic invasion, skin or nipple involvement. In summary, tumors in African American women were more likely to be to have characteristics associated with poor prognosis than were white women. explanatory variable. After adjustment for TNM stage at diagnosis, the factors that predict survival may be race specific.

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INTRODUCTION

This is a follow-up study of a cohort of African American and white women who were diagnosed with breast cancer in the late 1980s. The study aims are to examine race differences in survival, examine predictors of survival for all study subjects (controlling for race), and to identify race-specific predictors of survival. The primary objective is to identify factors that explain the observed race difference (African American/white) in survival from breast cancer. Factors to be evaluated include demographic variables, socioeconomic status, psychosocial factors, comorbidity, breast cancer treatment modalities, tumor characteristics, and specific genetic alterations.

PROGRESS TO DATE WITH RESPECT TO ORIGINAL STATEMENT OF WORK

Task 1: Month 1-1.5: Hire project coordinator/ **COMPLETED**

Task 2: Months 1-6: Submit protocol to 22 hospitals to gain approval from the Institutional Review Boards. This requires a significant amount of paperwork as well as personal appearances by the P.I. and the RCA director. **COMPLETED**

Task 3: Months 1-12: Develop and learn a data tracking system. This will be preceded by the purchasing of a new computer and appropriate software. **COMPLETED**

Task 4: Months 1-3: Review all existing files on patients to establish a comprehensive list of hospitals in which tumor specimens might be located. This is not a task that can be computerized, because the existing data is part of original documentation that was abstracted from patients' medical charts. **COMPLETED**

Task 5: Months 7-9: Collect tumor specimens from 22 hospitals. **COMPLETED**

UPDATE:
In this last year, we were successful at acquiring the tissue blocks (17 cases) from one hospital that had previously denied access. Two other hospitals (total of 6 cases) did not release blocks. By the end of December, 1999, we considered any uncollected specimens as missing data.

Task 6: Months 7-9: Link study cases to Connecticut Tumor Registry files. **COMPLETED IN 1997; DATA INCLUDED IN PRELIMINARY RESULTS PRESENTED AT ERA OF HOPE MEETING**

UPDATE:
All CTR data were updated in the early months of 1999. We completed the task of cleaning these data and supplementing outcome information when necessary. Specifically, the CTR does not list information on recurrence or time to recurrence. We developed a system for identifying cases that received therapy more than one year since the original diagnosis as a screen for recurrent cases.

Task 7: Months 9-12: Select from all available paraffin blocks on each patient, the best specimen (tumor block) for further testing. This will require a review of tumor slides (and preliminary staining) by the pathologist. **COMPLETED**

Task 8: Months 13-24: Laboratory testing on approximately 300 tissue samples. Tests to be done are the following: Histopathologic grade, tumor grade, estrogen receptors, progesterone receptors, DNA ploidy, S phase fraction, presence of p53 mutations, and overexpression of erbB-2. Additionally, gene sequencing will be done on all tumors that are positive for p53 in order to determine location and type of mutation. . **COMPLETED**

UPDATE:

The testing of Phospho-neu that was reported last year has not yielded meaningful results. Dr. Michael DiGiovanna, another DOD recipient from Yale, has plans to repeat some of this testing in the coming year. The cost of this testing was picked up by Dr. DiGioavanna's lab.

Task 9: Months 13-30: Review all original documentation (e.g., progress notes, M.D.consults, discharge summaries), patient interviews for available data on treatment for cancer. Compare these data with CTR data. Fill in the blanks: i.e., contact physicians, specialists, or patients in order to gain as complete information as is possible. **COMPLETED**

Task 10: Months 13-30: This task will be coordinated with task 8, in that a similar review of all available data will be conducted to ascertain vital status (including recurrence or development of subsequent primary cancer). **COMPLETED**

UPDATE, TASKS 9 AND 10: These tasks were repeated this year. Once the data analyses were underway, we had questions about the quality of the original data abstraction. The data now available for analyis has been validated using multiple sources of data.

Task 11: Months 12-18: Data Management. Even though the data will be "trickling" in over the next year and one-half, the development of SAS datasets will be underway well in advance of having completed data collection. This will involve the assimilation of several different data sources with existing data to develop SAS data sets, as well as creation of variables, and various indices (especially relevant to the psychosocial variables). **COMPLETED**

UPDATE: A PhD- level student biostatistician (Fenghai Duan) joined the study this year (Dr. Ta left the study). He doublechecked much of Dr. Ta's initial data management work. We found some errors in the existing data base. Because the errors were not systematic, we decided that we would repeat much of this work before proceeding with the data analysis. The data management tasks are now complete.

Task 12: Months 18-end of project period: Data Analysis. The timing of this task will depend on the availability of the data. Because of the scope of the proposed project, and the availability of existing data, it is reasonable to plan for data analyses even before all data are available.

UPDATE:
We are mid-way through the data analysis. New results were presented at the Era of Hope meeting in Atlanta. These new results are appear below, See: UPDATED FINDINGS. Because this is a very rich data source, we anticipate publishing many more findings than those presented to date.

Task 13: Year 04: Write-up of results. Clearly, the reporting of results needs to be done in conjunction with on-going analyses. Other than preliminary reports, we anticipate that the major write up will take place in the last year of the study.

UPDATE:
To be continued in Year 05, as new findings emerge.

Goals for the Upcoming Year

To begin, with the exception of major data analysis, all of the tasks outlined in last year's "Goals for the Upcoming Year" were accomplished. The primary activities to be accomplished in year 04 are data analysis and manuscript preparation. Additionally, there are some final lab tests to be performed (on the specimens from the 3 hospitals that have not yet provided tumor tissue), as well as final reading of the p-neu results and SSCP, DNA sequencing by the study pathologist. Additionally, there is a fairly large administrative task to be performed in that all tumor blocks and slides must be returned to the 22 participating community hospitals. Because we received many blocks and slides on each patient, and much of this material is still in the hands of several different laboratories, this task and continuing data management will be one of several tasks assigned to the project coordinator.

KEY RESEARCH ACCOMPLISHMENTS

Preliminary Findings:

- Established race difference in survival from breast cancer, after adjustment for stage at diagnosis

- Established race differences for a number of recognized prognostic indicators: African American women compared to white women are (significantly = *) more likely to have:

  *Later stage at diagnosis
  *Larger tumors
  *Positive lymph nodes
  *Higher histologic grade
  *Higher Nuclear grade
  *Estrogen Receptor Negative tumors
  Progesterone Receptor Negative tumors

- Established race differences for a number of genetic alterations that are associated with worse prognosis: African American women compared to white women are (significantly = *) more likely to have:

  *P53 positive tumors
  C-met positive tumors

Note: African American women were not more likely to be diagnosed with HER-2(neu) positive tumors.

- Established race differences for a number of known tumor characteristics that are thought to be associated with poorer prognosis, or at least later stage at diagnosis. Although African American women compared to white women were more likely to have each of the following, these are not statistically significant race differences.

- Survival differences across race groups persist even with adjustment for socioeconomic status (measured as Education)

Once analyses are completed, results will be published- we anticipate a number of publishable papers resulting from this investigation.

UPDATE OF PRELIMINARY FINDINGS

This is a population based follow-up study of 145 African American (AA) and 177 white (W) women who were diagnosed with breast cancer between January, 1987 and May, 1989. As of January, 1999, 135 (41.9%) of the women had died with an average time to death of 4.7 years. Eighty-seven (64.4%) of the deaths were confirmed breast cancer deaths. Among survivors, women were followed for a maximum of 11.6 years and an average of 9.2 years. Survival among AA women (56.9%) was significantly lower than survival in W women (68.9%) [age-adjusted Risk Ratio {RR} 1.73 (95% Confidence Interval {CI} 1.21 – 2.48)]. The significant survival disadvantage persisted even with
additional adjustment for TNM stage at diagnosis and one measure of socioeconomic status (education) (RR 1.49, 95% CI 1.02 – 2.19).

Several tumor characteristics differed by race group, with African American women more likely to be in the higher risk category. As we have previously reported, African American women were twice as likely to be diagnosed with tumors that were TNM stage II or higher (age-adjusted Odds Ratio [OR] = 2.01, 95% Confidence Interval [CI] 1.24 – 3.24). Evaluating archived tissue specimens, we have demonstrated race differences in a number of other tumor characteristics and genetic alterations: AA women were more likely than W women to have tumors that were higher histologic grade (age-adjusted OR 2.20, 95% CI1.08 – 4.49), higher nuclear grade (age-adjusted OR = 2.00, 95%CI 1.04 – 3.85), estrogen receptor negative OR = 1.82, 95% CI 1.09 – 3.03, and p53 positive (OR = 4.00, 95% CI 1.77 – 9.01), all of which are generally associated with relatively poor prognosis. Although AA women were more likely than W women to be progesterone receptor negative (61% vs. 50%), and to express c-met (62% vs. 56%), these differences were not statistically significant. AA women were not significantly more likely to be HER-2 [neu] positive. African American women were more likely (not significant) to be positive for a number of known prognostic indicators: necrosis, lymphatic invasion, skin or nipple involvement. Results suggest that after adjustment for TNM stage, only p53 (+) and skin involvement were predictive of survival in African American women, and histologic grade was predictive in White women. Neither c-met or HER-2 (neu) were significantly associated with survival in this population of women.

Summary: African American women were significantly more likely to die during the 10- year (approximate) follow-up period than were White women who had been diagnosed with breast cancer in Connecticut in the late 1980s. Tumors in African American women were more likely to be to have characteristics associated with poor prognosis than were white women. The race difference in TNM stage at diagnosis was the strongest explanatory factor for the observed race difference in survival. Race difference in socioeconomic status was not an important explanatory variable. After adjustment for TNM stage at diagnosis, the factors that predict survival may be race specific.

REPORTABLE OUTCOMES:

1) Abstract presented at 1997 Era of Hope meeting, Washington, DC

Race Differences (Black/White) in Breast Cancer Survival
Beth A. Jones, Ph.D, Meredith Glazer,, Ph. D. Stanislav V. Kasl

2)
Abstract presented at 2000 Era of Hope meeting, Atlanta, Georgia
Manuscript in preparation
Presentation to be delivered at APHA, November, 2000, Boston Mass

Race Differences in Tumor Related Prognostic Factors for Breast Cancer

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To date, there have been no other published or publicly presented abstracts from this investigation.

CONCLUSIONS:

At the end of year 04, results indicate that African American women were significantly more likely to die during the 10- year (approximate) follow-up period than were White women who had been diagnosed with breast cancer in Connecticut in the late 1980s. Tumors in African American women were more likely to be to have characteristics associated with poor prognosis than were white women. The race difference in TNM stage at diagnosis was the strongest explanatory factor for the observed race difference in survival. Race difference in socioeconomic status was not an important explanatory variable. After adjustment for TNM stage at diagnosis, the factors that predict survival may be race specific.

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